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REVIEW ARTICLE

From cancer treatment strategies to survivorship care: Advances in integrating multi-omics and artificial intelligence

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Abstract

Advances in oncology are successfully shifting clinical focus beyond initial tumor control to address the complex, lifelong needs of a growing survivor population. This review examines the evolution of therapeutic paradigms, dissecting the mechanistic underpinnings and clinical impact of modern immunotherapies and gene-based modalities. It further addresses the multifaceted challenges in survivorship care, from managing persistent morbidity and psychological distress to overcoming systemic barriers in care coordination. Central to this discussion is the promise of multi-omics—which offers a high-resolution lens into tumor and host biology—to enable preemptive risk profiling. Concurrently, artificial intelligence (AI) emerges as the computational engine to distill these complex datasets into actionable intelligence for personalized surveillance. Furthermore, this review explores the translational hurdles facing AI, with a critical examination of inherent vulnerabilities, such as algorithmic bias, model opacity, and ethical pitfalls, in clinical deployment. By synthesizing these domains, this article provides a conceptual framework to steer the evolution of evidence-based, equitable, and patient-focused survivorship care.

Keywords: Cancer treatment strategy; Cancer survivorship care; Multi-omics; Artificial intelligence; Personalized medicine

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1. Introduction

The management of cancer embodies a dynamic interplay between scientific innovation and evolving clinical imperatives. Grounded in the hallmarks of genomic instability and dysregulated cell proliferation, cancer continues to impose a significant global health burden, necessitating relentless refinement across the entire spectrum of oncological care, from prevention to long-term management.[1,2] The therapeutic arsenal has been fundamentally transformed over the past decades, moving decisively from broadly

cytotoxic regimens toward a precision medicine paradigm defined by molecularly targeted strategies.[3,4]

This shift finds a powerful exemplar in the rise of cancer immunotherapy. Modalities such as immune checkpoint inhibitors (ICIs), which disrupt pivotal suppressive pathways like programmed cell death 1/programmed death ligand 1, and the engineering of chimeric antigen receptor (CAR) T-cells, are designed to overcome tumor-mediated immune suppression and reinvigorate endogenous antitumor responses, yielding profound and durable remissions across diverse cancer types.[5,6] The strategic incorporation of these novel agents with conventional treatments has substantially augmented survival rates, thereby propelling the oncology community into a critical new era: the transition from acute, tumor-focused care to long-term, patient-centered survivorship care.[7]

Consequently, the global cohort of cancer survivors is expanding, presenting healthcare systems with a complex and escalating challenge.[8] Contemporary survivorship care constitutes a comprehensive, longitudinal endeavor focused on mitigating the long-term and late-onset effects of both the malignancy and its often-toxic treatments. Its core mandate spans the prevention of disease recurrence and secondary neoplasms, vigilant surveillance for a spectrum of physical and psychological sequelae, active intervention for symptom control, and seamless coordination between oncology specialists and primary care providers.[9,10] Prevailing care models, however, frequently prove inadequate in addressing profound physical morbidities (e.g., persistent fatigue, neuropathies, pain syndromes), significant psychological distress (e.g., anxiety, depression, fear of recurrence), and the pervasive socioeconomic burdens, including financial toxicity and challenges in social reintegration.[11,12] The development of integrated, evidence-based, and personalized survivorship frameworks is therefore an urgent priority to optimize functional outcomes and quality of life for this burgeoning population.

Within this context, the convergence of two technological frontiers—multi-omics and artificial intelligence (AI)—holds exceptional potential to bridge the gap between therapeutic breakthroughs and comprehensive survivorship. Multi-omics profiling, through the concerted application of genomics, transcriptomics, proteomics, and metabolomics, furnishes an unprecedented, holistic vista of both tumor pathophysiology and the individual's host environment.[13] This integrative approach facilitates a deeper interrogation of resistance mechanisms, unveils biomarkers predictive of late effects, and informs the creation of dynamic, personalized surveillance strategies anchored in individual risk.[14] In parallel, AI and machine learning (ML) provide the indispensable computational power to decipher the immense complexity inherent in multi-omics data, electronic health records, and medical imaging.[15] These tools are being leveraged to augment diagnostic acuity, forecast individual therapeutic responses and toxicities, automate administrative workflows to enhance care coordination, and empower patients through intelligent digital tools.[16]

The translation of these sophisticated technologies into routine clinical practice, however, is fraught with formidable challenges. The multi-omics field must contend with issues of data standardization, integrative bioinformatics, and consequential biological interpretation.[16,17] Similarly, the widespread adoption of AI is tempered by valid concerns regarding algorithmic bias, model interpretability (the "black box" problem), data privacy, and the imperative for robust, prospective clinical validation.[17,18] A critical and discerning evaluation is thus paramount to translate their considerable promise into tangible clinical benefit.

The successful transition from acute cancer therapy to long-term survivorship care unveils a critical gap: The lack of a systematic framework that integrates technological advances with persistent clinical and ethical challenges. This review is motivated by the urgent need to synthesize these disparate domains and guide the evolution of next-generation survivorship models. To this end, it makes four primary contributions. First, it synthesizes the mechanistic evolution of cancer therapeutics and delineates the complex landscape of survivorship challenges they have engendered. Second, it provides a critical appraisal of the synergistic roles of multi-omics profiling and AI in enabling precision survivorship care. Third, it analyzes the formidable technical, translational, and ethical hurdles that currently impede the routine clinical adoption of these technologies. Finally, it proposes a forward-looking roadmap to navigate these barriers, with the ultimate goal of steering the field toward evidence-based, equitable, and patient-centered survivorship care ecosystems.

This review is crafted for clinical oncologists, translational researchers, and digital health innovators seeking a nuanced perspective on the integrated future of cancer care. This review critically synthesizes advances in cancer therapeutics, delineates the intricacies of modern survivorship, and places particular emphasis on the synergistic roles of multi-omics and AI. Distinct from a merely descriptive compilation, this work furnishes a balanced appraisal of both the capabilities and constraints of these technologies, with the ultimate objective of guiding the creation of effective, equitable, and patient-centered oncology care models.

2. The evolution of modern cancer treatment strategies

The landscape of cancer intervention has been radically reconfigured, evolving from an era dominated by empirical cytotoxics to a new age defined by mechanism-driven therapeutics.[18] This transition mirrors a deeper comprehension of oncogenic processes, enabling the design of interventions with enhanced specificity and a more favorable therapeutic index, thereby accelerating the adoption of precision oncology.[18,19] The subsequent sections provide a critical appraisal of the foundational modalities that constitute modern cancer care, with a dedicated focus on their operational mechanisms and clinical implementation—advances that, in their success, inherently demand the concurrent development of sophisticated survivorship frameworks.

2.1. The immunotherapy revolution

2.1.1. ICIs

ICIs constitute a landmark achievement in oncology, functioning through the targeted disruption of intrinsic immune regulatory circuits. These biologic agents, primarily monoclonal antibodies, selectively antagonize inhibitory receptors, such as programmed cell death-1 and cytotoxic T-lymphocyte-associated protein 4, and molecular pathways frequently co-opted by malignancies to induce T-cell exhaustion and evade immune destruction.[20,21] By impeding these negative signals, ICIs reinstate potent antitumor immunity and have demonstrated remarkable, durable clinical activity across a spectrum of cancers, including melanoma and non-small cell lung carcinoma.[22,23] Nonetheless, their application is circumscribed by heterogeneous response patterns and a unique spectrum of immune-related adverse events, underscoring the pressing need for reliable predictive biomarkers and refined patient selection algorithms.[24,25] While ICIs represent a paradigm shift, their clinical utility is constrained by unpredictable efficacy and toxicity. Future development hinges on the discovery of robust composite biomarkers that integrate tumor genomics with host immune contexture to guide personalized application.

2.1.2. Adoptive cell transfer

Adoptive cell transfer represents a pinnacle of personalized cancer immunotherapy, epitomized by CAR-T therapy. This sophisticated modality involves the genetic reprogramming of a patient's own T lymphocytes to express synthetic receptors that target specific tumor-associated antigens, such as CD19 in B-cell malignancies.[26,27] The process generates a potent, expanded population of cytotoxic T-cells capable of mediating antigen-directed tumor cell lysis. Successive iterations of CAR-T constructs have incorporated co-stimulatory domains (e.g., CD28, 4-1BB) to augment their *in vivo* persistence and cytotoxic efficacy.[28,29] In a complementary approach, T-cell receptor-engineered T-cell therapy leverages the specificity of natural T-cell receptors to recognize intracellular tumor antigens presented by major histocompatibility complexes, showing considerable promise for targeting solid tumors.[30,31]

2.2. Gene therapy: A vectorized approach

Recombinant adeno-associated virus has emerged as a leading vector platform for *in vivo* gene delivery in oncological applications, prized for its favorable safety profile and capacity for sustained transgene expression.[32,33] Engineered recombinant adeno-associated virus vectors can be armed with a diverse array of therapeutic transgenes—encoding entities such as tumor suppressors, anti-angiogenic factors, and immunomodulatory cytokines—for direct localized delivery to tumor sites.[34,35] This strategy of *in situ* gene transfer enables the targeted production of biologic agents within the tumor microenvironment, minimizing systemic exposure and potentially bypassing conventional drug resistance mechanisms. Contemporary research is concentrated on refining vector tropism to enhance tumor selectivity and overcoming the challenge of pre-existing neutralizing antibodies in patient populations.[36,37]

2.3. Molecular targets as therapeutic levers

The development of molecularly targeted agents represents a cornerstone of precision oncology, focusing on the specific pathways that fuel tumorigenesis.[19] The clinical deployment of these agents, however, reveals a complex interplay of opportunity and challenge. For instance, while dysregulation of the human epidermal growth factor receptor (HER) tyrosine kinase network provides a compelling therapeutic rationale in cancers such as HER 2-amplified breast and gastric carcinomas, the efficacy of targeted inhibitors is frequently constrained by adaptive pathway reactivation and acquired resistance mutations.[38,39] Similarly, targeting the NOD-, LRR-, and pyrin domain-containing protein 3 (NLRP3) inflammasome presents a unique conundrum due to its context-dependent role in tumorigenesis—where it can promote progression in some malignancies while exerting antitumor effects in others, necessitating meticulous patient stratification.[40,41] This functional duality represents a significant unresolved debate, complicating the development of NOD-, LRR-, and pyrin domain-containing protein 3-targeted therapies and underscoring the need for precise biomarkers to stratify patients based on tumor context. Furthermore, cancer stem cells persist as a formidable therapeutic barrier,

implicated in treatment resistance and disease relapse. These cells are maintained by evolutionarily conserved developmental pathways, such as Wnt/β-catenin and Hedgehog signaling, suggesting that their targeted disruption may be indispensable for achieving durable disease control.[42,43]

2.4. Synthesis and forward perspective

The collective progress in immunotherapy, gene therapy, and molecularly targeted agents has fundamentally recalibrated the management of cancer. The strategic deployment of these modalities, particularly within rational combination regimens, has markedly improved clinical outcomes across a diverse range of malignancies.[6,44] This very therapeutic success, however, has engendered a new set of challenges, giving rise to a growing and complex population of survivors with multifaceted long-term needs.[7]

3. The landscape and challenges of cancer survivorship care

The remarkable achievements in cancer therapeutics, while unequivocally improving survival trajectories, have concurrently unveiled a new dimension of clinical complexity: the long-term management of cancer survivorship. As this global population continues to expand, healthcare systems are confronted with the intricate task of addressing multifaceted needs that extend far beyond the conclusion of primary anticancer treatment.[7] Modern cancer survivorship care embodies a holistic, proactive approach dedicated to monitoring and alleviating the long-term and late-arising consequences of cancer and its treatments, promoting overall health, and optimizing quality of life across the entire survivorship continuum.[8]

The architecture of contemporary survivorship care is built upon four foundational pillars: first, the prevention of recurrent and second primary cancers; second, systematic surveillance for cancer recurrence and the detection of late-onset complications; third, active intervention for consequences related to cancer and its treatment; and fourth, coordinated care between oncology specialists and primary care services to ensure continuity and comprehensiveness.[9] This structured paradigm acknowledges survivorship as a distinct and prolonged phase of the cancer journey, demanding specialized knowledge, protocols, and resources to effectively address its unique challenges.

The clinical reality for survivors is often marked by a constellation of diverse and persistent issues. Physical sequelae represent a significant burden, with a high prevalence of cancer-related fatigue, chemotherapy-induced peripheral neuropathy, chronic pain conditions, and various organ-specific toxicities that can profoundly impair daily functioning and diminish quality of life.[10] In parallel, psychological distress manifests as clinically significant anxiety, depression, and particularly, the fear of cancer recurrence—a pervasive concern that can persist indefinitely after active treatment ends, casting a long shadow over a survivor's life.[11] These clinical challenges are frequently compounded by socioeconomic determinants, most notably financial toxicity stemming from treatment-related expenses, employment disruption, and ongoing healthcare costs, which collectively erect substantial barriers to accessing optimal survivorship care.[45]

Systemic and infrastructural barriers further impede the effective delivery of survivorship care. The transition from active treatment to long-term follow-up represents a critically vulnerable period, often characterized by fragmented communication and poorly defined care responsibilities between oncology specialists and primary care providers.[46] A scarcity of standardized, evidence-based protocols for monitoring and managing late effects, coupled with insufficient clinician training and education regarding survivorship care, frequently leads to the suboptimal recognition and management of treatment-related complications. Moreover, prevailing care models often fail to adequately conceptualize and address the intricate interplay between the physical, psychological, and social determinants that collectively define the survivor experience.[47] These multifaceted challenges underscore the critical imperative for innovative, scalable, and personalized approaches to survivorship care. The development of integrated, evidence-informed frameworks that strategically leverage emerging technologies represents an urgent and non-negotiable priority within modern oncology.

4. The integrative role of multi-omics in cancer survivorship care

The transformative success of contemporary cancer therapies has catalyzed the emergence of a growing survivor population confronting distinct long-term health challenges. While traditional surveillance paradigms remain heavily reliant on imaging and symptomatic presentation, multi-omics technologies are poised to redefine precision survivorship through comprehensive molecular phenotyping. This integrative methodology, which concurrently analyzes genomic, transcriptomic, proteomic, and metabolomic data, generates dynamic molecular signatures capable of guiding individualized survivorship management strategies.[12,13]

4.1. Molecular profiling for recurrence risk stratification

The assimilation of multi-omics data enables a sophisticated recalibration of risk assessment in cancer survivors through advanced molecular surveillance. The analysis of circulating tumor DNA (ctDNA) has emerged as a powerful tool for detecting minimal residual disease (MRD), with substantial evidence demonstrating its capacity to identify molecular recurrence with a significant lead time compared to conventional radiological modalities.[48] For instance, in early-stage non-small cell lung cancer, patient-specific phylogenetic ctDNA profiling after surgery detected MRD with a median lead time of 70 days before radiographic relapse. In this study, 93% (13/14) of patients who later experienced clinical recurrence had detectable ctDNA post-operatively, highlighting the high predictive value of ctDNA-based MRD assessment for impending relapse.[48] This utility is further evidenced by studies utilizing methylation signatures[49] and multi-analyte approaches[50] for sensitive cancer detection.

The predictive utility of ctDNA monitoring is further strengthened when integrated with other molecular analytes. Integrated interrogation of DNA methylation patterns with fragmentomic characteristics in cell-free DNA enhances sensitivity for early recurrence detection across multiple cancer types.[49] Furthermore, the incorporation of protein biomarker profiles alongside ctDNA quantification yields complementary information that refines risk stratification, proving particularly valuable in early-stage diseases where ctDNA abundance may be minimal.[50]

Beyond liquid biopsies, tissue-based multi-omics approaches furnish unique insights into recurrence mechanisms. Spatial transcriptomic profiling of histologically normal adjacent tissues reveals molecular field effects that may predispose to local recurrence,[51] while proteomic characterization of the tumor microenvironment uncovers immune contextures associated with durable treatment responses.[52] Single-cell RNA sequencing further delineates the cellular heterogeneity within residual disease populations, identifying transcriptional programs correlated with metastatic competence.[53]

The full potential of multi-omics is realized through the integration of these disparate data types via advanced computational methodologies. ML algorithms can synthesize genomic, transcriptomic, and proteomic features to generate composite recurrence risk scores that outperform predictions grounded solely in clinicopathological parameters.[54] Nevertheless, the clinical translation of these integrated models confronts substantial hurdles, including technical batch effects across omics platforms, the necessity for large, meticulously annotated cohorts for algorithm training, and the biological interpretation of complex, algorithmically-derived signatures. These sophisticated models facilitate genuinely personalized surveillance approaches, optimizing monitoring intensity and modality based on individual molecular risk profiles rather than population-derived guidelines.[55] The promise of multi-omics in recurrence risk stratification is clear, yet its clinical translation remains in early stages. Widespread adoption requires not only technical standardization and cost reduction but also prospective validation proving that risk-adapted surveillance improves survival or quality of life compared to standard follow-up.

4.2. Prediction and management of long-term treatment-related complications

Multi-omics approaches are revolutionizing the prediction and management of treatment-related sequelae through comprehensive molecular profiling of individual susceptibility and incipient pathological processes.[12] Pharmacogenomic investigations have identified numerous genetic variants that modulate vulnerability to specific treatment toxicities, enabling risk-adapted therapeutic selection and tailored surveillance strategies.[56] A prime example is a coding variant in the *RARG* gene (rs2229774), which has been robustly associated with a significantly increased risk of anthracycline-induced cardiotoxicity in childhood cancer survivors, illustrating how pre-emptive genotyping can guide personalized therapy and monitoring strategies.[56] Recent advances in genome-wide association studies have substantially expanded our understanding of the genetic architecture underlying complications such as chemotherapy-induced neurotoxicity and radiation-induced tissue damage.[57]

Metabolomic profiling delivers a dynamic readout of physiological perturbations following oncological treatments, offering distinctive insights into the mechanisms of long-term complications. Characteristic metabolic signatures have been discerned for diverse treatment-related toxicities.[58] Analogously, proteomic analyses reveal circulating biomarkers that reflect ongoing processes of tissue injury and repair, creating opportunities for pre-emptive detection and intervention.[59] In childhood cancer survivors, exercise intolerance—as measured by low peak oxygen uptake—is prevalent and is associated with all-cause mortality, with hazard ratios as high as 3.93 (95% confidence interval: 1.09–14.14). Impaired organ systems, including cardiac (e.g., abnormal global longitudinal strain), autonomic (chronotropic incompetence), pulmonary (forced expiratory volume in 1 s < 80%), and muscular (reduced quadriceps strength), contribute to this intolerance, underscoring the potential role of multimodal

biomarker assessment in identifying high-risk survivors for targeted intervention.[59]

The convergence of multiple omics layers generates compelling insights for complex conditions, such as cancer therapy-related cardiac dysfunction.[60] Combined genomic, proteomic, and metabolomic profiling has delineated distinct molecular subtypes of cardiac injury, each possessing characteristic biomarker signatures and clinical trajectories.[60] These refined molecular classifications enable more targeted monitoring and preventive strategies predicated on the specific pathophysiological processes active in individual patients.[61]

The preceding analysis delineates the independent potential of genomics, transcriptomics, proteomics, and metabolomics in elucidating the molecular foundations of survivorship outcomes. However, the translation of this multidimensional data into clinically actionable insights necessitates a robust computational scaffold. As illustrated in Figure 1, the integration of these heterogeneous multi-omics data streams constitutes the foundational input for AI models, which function as the central analytical engine for prediction and inference.

4.3. Translational hurdles: Cost, feasibility, and accessibility

Despite its transformative potential, the widespread integration of multi-omics into routine survivorship care faces substantial practical barriers, with cost, feasibility, and accessibility constituting the most significant clinical hurdles.

Cost remains a primary obstacle. Comprehensive multi-omics profiling—encompassing whole-genome sequencing, transcriptomics, proteomics, and metabolomics—carries a high financial burden. While costs are decreasing, they are still prohibitive for most healthcare systems outside of research settings, and reimbursement mechanisms are underdeveloped. The economic case for widespread adoption relies on demonstrating not just clinical utility, but also long-term cost-effectiveness through prevented recurrences and reduced late-effect management.

Feasibility challenges span the entire workflow. Pre-analytical variables such as sample collection, processing, and storage require stringent standardization to ensure data quality and reproducibility across different centers. The analysis and interpretation of multi-omics data demand specialized bioinformatics expertise, which is scarce in many clinical environments. Integrating these complex data streams into existing electronic health records and clinical decision support systems presents further technical and operational complexities.

Accessibility concerns threaten to exacerbate existing health disparities. The infrastructure and expertise required for advanced omics profiling are concentrated in large, academic tertiary care centers. This creates an "omics divide," where survivors treated in community or rural

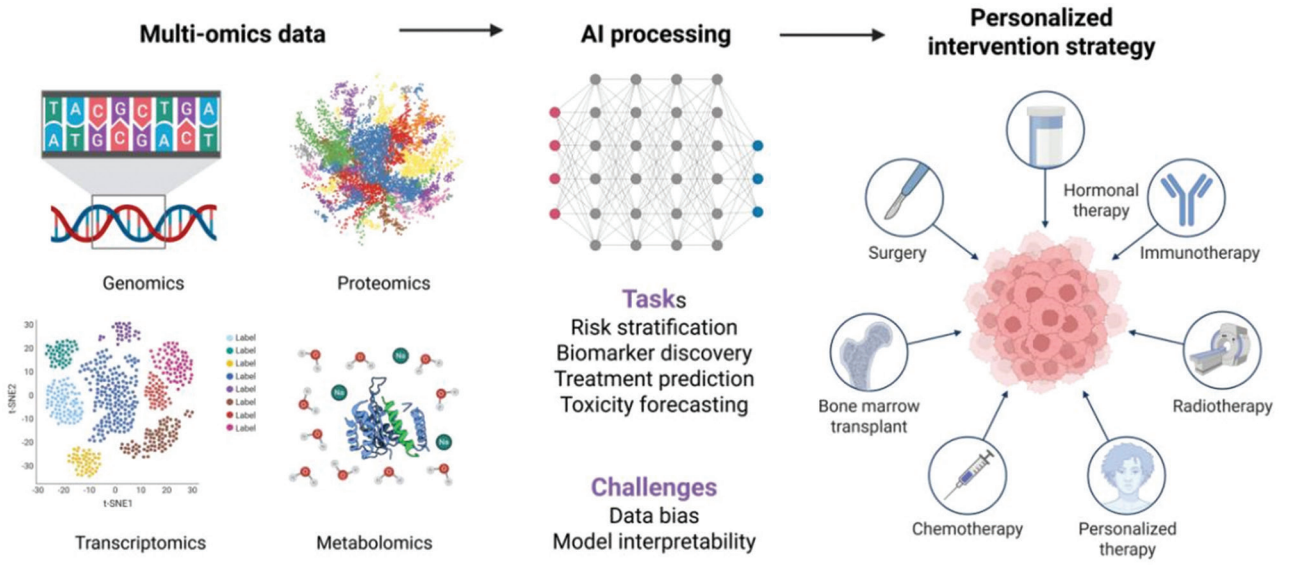

Figure 1. A conceptual framework for AI and multi-omics in survivorship care. This schematic outlines the pathway from multi-omics data acquisition to computational analysis and the subsequent delivery of personalized SCPs. The AI processing stage highlights central analytical tasks while acknowledging prevailing limitations. The final output enables precision interventions tailored to the individual survivor's dynamic molecular risk profile. Created with BioRender.com, Ling Yin (2026), https://app.biorender.com/illustrations/68e4bbdd87048e01114d2269.
Abbreviations: AI: Artificial intelligence; SCPs: Survivorship care plans.

settings, or in low- and middle-income countries, may not have access to these precision tools. Without deliberate policy interventions, equitable access frameworks, and the development of simplified, point-of-care omics technologies, the promise of precision survivorship risks becoming a privilege for the few, rather than a standard for all.

Addressing these translational hurdles is therefore not a secondary concern but a prerequisite for the ethical and sustainable implementation of multi-omics in cancer survivorship. Future efforts must prioritize the development of cost-effective assays, automated analysis pipelines, and scalable delivery models that can extend the benefits of molecular profiling to diverse and underserved survivor populations.

5. The integration of AI into cancer survivorship care

The inadequacy of conventional, generalized survivorship models necessitates a fundamental transition toward precision care. In this context, AI arises as a transformative enabler. Augmenting the foundational data derived from multi-omics, AI supplies the computational prowess to decode profound complexity, forecast individual risks, and automate care processes, thereby bridging the chasm between innovative therapy and comprehensive long-term wellness (Figure 1).

5.1. AI in multi-omics data integration and biomarker discovery

The molecular underpinnings of recurrence risk and late effects, as elucidated through multi-omics, yield datasets of immense intricacy. AI and ML are becoming indispensable for distilling this information into clinically actionable intelligence.

A primary application lies in the fusion of disparate omics layers—genomic, transcriptomic, proteomic, metabolomic—to construct unified predictive models. Deep learning architectures are capable of identifying non-linear interactions between diverse molecular features that remain opaque to conventional statistical methods. For instance, ML models can amalgamate somatic mutation profiles with plasma proteomic data to generate a composite risk score for recurrence that significantly surpasses the predictive performance of models based solely on clinical parameters.[13] Furthermore, AI demonstrates exceptional proficiency in *de novo* biomarker discovery. In the analysis of cell-free DNA, ML algorithms can not only detect the presence of ctDNA but also harness fragmentomic patterns and methylation signatures to predict MRD and imminent relapse with superior sensitivity and lead time compared to standard techniques.[48,49] AI can also be deployed to anticipate specific late effects; for example, by analyzing pre-treatment genomic data and on-treatment metabolomic shifts, models can stratify patients according to their risk for chemotherapy-induced cognitive impairment or cardiotoxicity, enabling preemptive interventions.[56,58] A critical limitation, however, is that many of these AI-discovered biomarkers and models remain associative rather than demonstrative of causation. Their clinical adoption, therefore, hinges on subsequent rigorous biological validation in independent cohorts and functional studies to elucidate the underlying mechanisms, ensuring they reliably guide clinical decision-making. This underscores a fundamental tension in AI-driven discovery: the trade-off between identifying powerful statistical associations and establishing biologically causal, mechanistically interpretable relationships—a debate central to the field's credibility and clinical translation. AI is pivotal for unlocking patterns within complex multi-omics data, moving beyond simple association toward predictive modeling. However, the field must evolve to develop more efficient, interpretable, and biologically grounded models to ensure robust clinical translation.

5.2. Automated monitoring of late effects in radiology and pathology

Many long-term consequences of cancer therapy manifest as structural alterations in organs, detectable through medical imaging and histopathological examination. AI-powered computer vision is redefining the surveillance of these sequelae.

In radiology, radiomics—the high-throughput extraction of quantitative features from medical images—facilitates the objective and sensitive monitoring of tissue damage. For instance, a deep learning model can be trained to automatically quantify the progression of radiation-induced pulmonary fibrosis on serial chest computed tomography scans, tracking subtle changes long before they become discernible to the human eye. Similarly, in cardio-oncology, AI algorithms applied to echocardiograms or cardiac magnetic resonance imaging can precisely measure myocardial strain, enabling the early identification of subclinical cardiac dysfunction in survivors exposed to cardiotoxic agents such as anthracyclines or HER 2-targeted therapies.[60] In digital pathology, AI models perform automated "digital biopsies." These systems can screen histopathological slides for specific treatment-related toxicities, such as identifying features of immunotherapy-related colitis in colon biopsies or drug-induced liver injury in liver biopsies, thereby offering a scalable tool for systematic tissue-level surveillance.[62] It is crucial to note, however, that the regulatory approval and

routine clinical deployment of such AI tools significantly lag behind their technical development. A key barrier is the necessity for prospective, randomized trials to conclusively demonstrate that AI-driven monitoring leads to improve patient outcomes, such as reduced morbidity or enhanced quality of life, rather than merely increasing the detection of incidental findings. AI-driven image analysis offers a robust, objective method for tracking subclinical organ damage. Bridging the gap from technical promise to proven clinical benefit is the paramount challenge, demanding trials that measure impact on patient-centric outcomes, not just algorithmic performance.

5.3. AI-powered risk stratification and personalized care plan generation

The transition from active treatment to survivorship is a critical juncture that demands personalized planning. AI moves beyond static guidelines by generating dynamic, individual-specific SCPs.

The power of AI here lies in data fusion and dynamic updating. ML models can synthesize a patient's complete history—including tumor type and stage, treatment modalities and cumulative doses, genomic susceptibility variants, current comorbidities, and real-time patient-reported outcomes—to generate a dynamic risk profile. This profile estimates the personalized probability of recurrence, second primary cancers, and specific late effects (e.g., fatigue, anxiety, lymphedema). This computational risk assessment can then directly inform the SCP. For example, an AI system could automatically generate a tailored plan recommending: a specific imaging surveillance schedule based on recurrence risk; a customized exercise regimen to combat fatigue; and targeted screening for psychological distress based on the patient's profile.[63,64] Emerging applications of large language models can further translate these structured recommendations into an easy-to-understand, patient-facing SCP document, improving health literacy and adherence.[65,66]

5.4. AI tools for patient self-management and remote monitoring

Effective survivorship care extends beyond the clinic into the patient's daily life. AI-driven digital health tools are empowering survivors and creating a continuous feedback loop between patients and their care teams.[15]

Conversational AI agents and chatbots provide 24/7 access to vetted information and support. They can answer questions about medication side effects, diet, and managing common symptoms such as pain or nausea. More advanced systems can conduct proactive check-ins, using natural language processing to screen for worsening symptoms or psychological distress (e.g., fear of cancer recurrence) and escalating alerts to human providers when necessary.[67,68] When integrated with data from wearable devices (e.g., smartwatches), AI algorithms can monitor physiological parameters such as heart rate, sleep patterns, and activity levels. Deviations from an individual's baseline can serve as early warning signs for complications, such as arrhythmias, infections, or decompensating heart failure, facilitating timely intervention.[69]

The applications of AI and multi-omics discussed herein present a promising yet uneven landscape for addressing the diverse challenges in cancer survivorship. Table 1 provides a synthesized and critical overview, mapping specific survivorship challenges to their corresponding technological solutions, and crucially, evaluating the current level of evidence and primary limitations associated with each approach. This summary underscores that while some applications, such as ctDNA-based recurrence monitoring, are advancing toward clinical adoption, others remain primarily in the research or conceptual phase, facing significant technical and translational hurdles.

6. Challenges and future perspectives

Despite the compelling potential of integrated multi-omics and AI, their trajectory toward widespread clinical integration is fraught with formidable challenges that warrant acknowledgment. Transitioning from robust proof-of-concept to routine practice mandates overcoming a complex array of technical, translational, and ethical hurdles.

Notwithstanding these present impediments, the overarching ambition of this technological convergence is to inaugurate a fundamentally new paradigm for cancer survivor care. As conceptualized in Figure 2, we envisage a future centered on an AI-driven, dynamic closed-loop ecosystem for precision survivorship. This intelligent system transcends the limitations of a static, one-time plan by evolving into a self-refining learning entity that perpetually optimizes itself through continuous data assimilation, ensuring clinical decisions remain precisely synchronized with the survivor's evolving health status and individual needs.

This conceptual model illustrates the continuous cycle of data aggregation (Figure 2A), AI-powered analytics (Figure 2B), personalized intervention delivery (Figure 2C), and real-world monitoring with feedback (Figure 2D). Multi-omics and clinical data are integrated to enable risk prediction and personalized recommendations under human oversight and an ethical framework. The system dynamically refines care plans based on adherence tracking, symptom changes, and outcome measurements,

Table 1. Multi-omics and AI in cancer survivorship care: Applications and translational challenges

Survivorship care challenge	Multi-omics and data enablers	AI applications	Key limitations
Recurrence and second cancers	Circulating tumor DNA analysis; integrated genomic and epigenomic signatures; proteomic and metabolomic profiling	Machine learning models for dynamic risk stratification by integrating multi-omics and clinical data; deep learning for biomarker discovery from complex data	High cost and lack of standardized assays limit widespread adoption; prospective trials are needed to confirm that AI-driven interventions improve patient outcomes
Physical sequelae	Pharmacogenomic variants for toxicity susceptibility; metabolomic and proteomic profiles for early pathophysiological changes	Natural language processing for automated toxicity extraction and grading from electronic health records; computer vision for subclinical organ dysfunction detection in medical images	Predictive models are primarily associative and lack causal validation; performance and generalizability can be poor in underrepresented patient populations
Psychological distress	Polygenic risk scores for anxiety and depression; proteomic biomarkers of chronic stress response	Natural language processing for screening psychological distress from patient-reported outcomes and clinical notes; conversational AI agents for scalable support and triage of at-risk patients	Raises significant ethical and data privacy concerns; risk of algorithmic bias and requires rigorous human clinical oversight
Fragmented care coordination	Structured data from electronic health records on treatment history and comorbidities	Automated generation of personalized survivorship care plans using large language models; predictive analytics for care pathway optimization and resource allocation	Faces significant integration barriers with the existing healthcare information technology infrastructure; regulatory pathways for the clinical use of autonomous AI tools are unclear

Abbreviation: AI: Artificial intelligence.

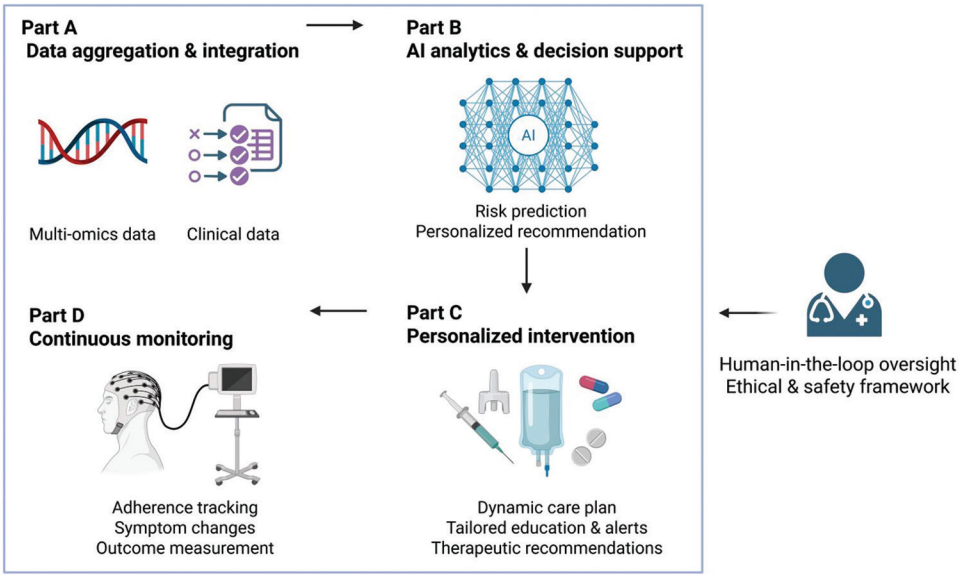

Figure 2. (A-D) A dynamic closed-loop framework for AI-driven precision survivorship care. Created with BioRender.com, Ling Yin (2026), https://app.biorender.com/illustrations/68e4ea8cea42bbf99d5bad06.
Abbreviation: AI: Artificial intelligence.

ensuring adaptive and patient-centered survivorship management.

6.1. Technical and analytical hurdles

The field of multi-omics must overcome issues of data standardization across different sequencing platforms and laboratories, and the computational complexity of integrative analysis.[16] For instance, harmonizing genomic variants called from different pipelines or integrating transcriptomic data from fresh-frozen versus formalin-fixed paraffin-embedded tissues remains a non-trivial challenge. For AI, the "black box" problem—where model decisions are not easily interpretable by clinicians—remains a significant barrier to trust and adoption.[17] This

creates a core contradiction: the most complex, high-performing models (e.g., deep neural networks) are often the least interpretable, forcing a difficult choice between predictive accuracy and clinical transparency. Without insight into the reasoning behind an AI's prediction of high recurrence risk, a clinician may justifiably hesitate to act upon it. Furthermore, AI models are highly susceptible to data bias; if trained on non-representative populations (e.g., predominantly of European ancestry or from tertiary care centers), they can perpetuate and even exacerbate existing healthcare disparities when deployed in more general settings.[70]

6.2. Clinical translation and ethical implementation

The transition from research to clinical practice requires robust, prospective validation in diverse patient cohorts to prove efficacy and cost-effectiveness. A model that predicts cardiotoxicity in a retrospective dataset must be validated in a prospective trial to see if it truly enables preemptive interventions that preserve cardiac function. Key implementation barriers include inadequate digital infrastructure in community oncology practices, data privacy concerns governing the sharing of sensitive multi-omics and health data, and the lack of regulatory frameworks tailored to adaptive AI systems that learn and evolve. This highlights a critical, unresolved debate: balancing the imperative for large, diverse datasets to train robust and equitable AI models against the equally vital need to protect patient autonomy and confidentiality. Ethically, the deployment of these technologies must be guided by principles of equity and transparency, ensuring that they augment, rather than replace, the clinician–patient relationship. This includes establishing clear accountability for AI-assisted decisions and ensuring that these tools do not widen the gap in cancer outcomes between affluent and underserved populations.[71]

6.3. A roadmap for the future: From integration to implementation

The future of cancer survivorship care lies not only in the synergistic convergence of therapeutic advances, deep molecular profiling, and intelligent computation but also in creating a sustainable ecosystem for their implementation. To this end, we propose a focused roadmap. First, prioritizing the development of explainable AI—a dedicated subfield aimed at solving the "black box" problem—is crucial. Explainable AI systems are designed to provide clinically intuitive justifications for their outputs, such as highlighting the specific genomic variants or imaging features that most contributed to a risk prediction.[72] Second, actively fostering interdisciplinary collaboration through shared funding initiatives and the creation of "translational triads" that bring together oncologists, data scientists, and bioethicists at the project inception stage. Finally, shifting the research paradigm to prioritize large-scale, pragmatic clinical trials that measure the real-world impact of these integrated approaches on patient-centric outcomes, such as quality of life, functional status, and financial toxicity.[73] By adhering to this roadmap, the field can transform the current promise into a tangible reality: The establishment of evidence-based, equitable, and patient-centered survivorship models that are as sophisticated and precise as the cancer treatments that made them necessary.

7. Conclusion

The oncology paradigm is undergoing a fundamental reorientation, shifting from a narrow focus on tumor eradication to a comprehensive framework dedicated to long-term survivorship care. This review has charted this evolution, underscoring how mechanistic breakthroughs in immunotherapy, gene therapy, and targeted agents have successfully created a large and growing population of survivors, thereby unveiling a complex new landscape of long-term and late-onset sequelae. In confronting these challenges, the integration of multi-omics data and AI has emerged as a cornerstone for the next generation of precision medicine. Multi-omics profiling furnishes a high-resolution, dynamic molecular portrait of the individual, elucidating the biological underpinnings of recurrence risk and treatment-related complications. Concurrently, AI provides the essential computational framework to distill these complex datasets into clinically actionable intelligence, enabling dynamic risk stratification, personalized surveillance protocols, and preemptive management strategies.

The translation of this technological potential into routine clinical practice, however, is contingent upon overcoming significant translational barriers. Foremost among these are the imperatives of ensuring robust data standardization, mitigating algorithmic bias to promote health equity, resolving the "black box" problem through explainable AI, and securing rigorous prospective validation of these tools against meaningful patient-centric outcomes. The objective is not the supplanting of clinical judgment but the creation of a synergistic, human-in-the-loop paradigm wherein data-driven insights augment clinical expertise to facilitate more informed and personalized decision-making.

In perspective, the future of cancer survivorship lies in the construction of a learning, adaptive healthcare system. The convergent application of therapeutic innovation, deep molecular phenotyping, and advanced computation

holds the promise of transitioning survivorship care from a one-size-fits-all model to a dynamic, lifelong state of personalized health management. Realizing this vision mandates a concerted, interdisciplinary endeavor that unites oncologists, computational biologists, clinical trial specialists, and bioethicists. The ultimate metric of success for this integrated approach will be its demonstrable capacity to optimize the quality of survival, ensuring that advancements in cancer therapy translate directly into sustained well-being for the global community of survivors.

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Conflict of interest

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